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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/686,619	10/17/2003	Margot Mary O'Toole	WYE-029	9490

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EXAMINER	
SALMON, KATHERINE D	

ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 10/686,619	Applicant(s) O'TOOLE ET AL.	
	Examiner Katherine Salmon	Art Unit 1634	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 08 December 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *None*.
   Claim(s) objected to: *None*.
   Claim(s) rejected: *1,2,5,8 and 22*.
   Claim(s) withdrawn from consideration: *4*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
    See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

Katherine Salmon, Examiner
Art Unit 1634

Continuation of 11. does NOT place the application in condition for allowance because: The reply asserts that the mouse model used in the instant specification shows that midkine expression levels are indicative of a likelihood of lupus therefore enabling diagnostic methods (p. 7 1st full paragraph). The response asserts that the mouse model is accepted by those of ordinary skill in the art as a means to generate data relevant to human biology (p. 7 2nd to last paragraph). The reply asserts that if an animal model is correlated to a specific human condition then the model is an "working example" (p. 7 last paragraph). The reply asserts that only an elevated expression is need to be indicative of an increased likelihood of lupus (p. 8 2nd to last paragraph). The reply asserts the mouse and human expression need not have the same level of expression (p. 8 2nd to last paragraph). The reply asserts that population stratification is involved in genetic association studies in humans but are not required for the use of midkine expression levels to be diagnostic. The reply asserts that though Lupus is complex, there is no genetic linkage analysis in the claims, only that midkine expression levels are indicative of a likelihood of lupus. These arguments have been fully considered but they are not found persuasive.

It is noted that the claims are drawn to a diagnostic method whereas the reply asserts a correlation of increased expression level with an "increased likelihood of lupus". Though mouse models can show data relevant to human biology, the prior art states that "different genetic contributions are operative in different animal models" (p. 7 of Final mailed 9/08/2006). Further, the models are used to study genetic causes of lupus, however environmental factors show considerable variation in lupus (p. 7 of Final). Therefore, though mouse models can show an genetic association of a gene with disease they are insufficient to correlate a gene expression with a diagnosis of the disease. The mouse model, would not be a "working example" of a diagnostic method only an example of an association of a disease and expression of a gene.

The reply asserts that elevated expression is indicative of an increased likelihood of lupus. The rejection made in the Final was asserting that the claims are drawn to ANY increase expression level, whereas, it seems that based on natural variations, there would be some increase expression in certain samples. Therefore with only the mouse model, it is unclear how high the expression levels must be in a human sample to diagnosis lupus.

Population stratification would play a role in a expression assay to diagnose lupus. It is unclear by the specification and the art if expression level of the midkine gene in humans are all similar or if different ethnic groups have different expression levels. Further, it is unclear is expression level is the same in male and female, since lupus is predominately in females. It is unclear if there are any other factors, which increase expression level.

The reply asserts that midkine expression levels are indicative of a likelihood of lupus, however, the claims are drawn to diagnosing Lupus based on elevated expression levels. It is unpredictable that any increase in expression would be correlative to a diagnosis of Lupus in any human population.

BJ FORMAN, PH.D.
PRIMARY EXAMINER